REMARKS

Claims 1-29 and 61-68 are pending in this application. Claims 30-50 and 60 have previously been canceled and claims 51-59 are being canceled without prejudice or disclaimer. Claims 22-29 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 61-68 have been added.

Claim 1 has been amended to amend subparts (b) and (c) and to insert new subpart (e). The numbering of the remaining subparts have been adjusted accordingly. As amended, subparts (b), (c) and (e) of claim 1, and claims 2, 7, 8, and 26 are directed to an albumin fusion protein wherein the albumin fragment is sufficient to prolong the serum half-life of interferon alpha protein, compared to the serum half-life of interferon alpha protein in an unfused state. Support for the amendments can be found, for example, on page 88 of the instant specification, lines 22-25; Example 4, particularly at page 212, lines 4-6, and Figure 7. Therefore, the amendments to claims 1, 2, 7, 8, and 26 are fully supported by the specification.

Of the withdrawn claims, claims 23-26 have been amended and claims 61-68 have been added herein to facilitate rejoinder. As amended, claims 23, 25, and 61-68 recite specific diseases or disorders as supported by Table 1, page 28, in column "Preferred Indication Y." Claim 24 has been amended to recite "an interferon alpha protein" instead of "Therapeutic protein X." Claim 26 has been amended as explained above. Claims 1-21 (pertaining to interferon alpha) are under examination. Applicants appreciate the Office's indication that claim 12 is allowable but objected to as being dependent on a rejected base claim.

Applicants respond to each issue raised in the Office Action dated June 22,

2004.

Correspondence Address

Applicants filed on September 22, 2003, a change of correspondence address. Accordingly, Applicants respectfully request that the Office mail all future correspondence to Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., 1300 I St. NW, Washington DC, 20005.

Rejection Under 35 U.S.C. § 112

Claims 1-4 and 13-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office contends that the word "has" is missing in section b of claim 1 in the phrase ". . . wherein said fragment has the ability to prolong the shelf life of interferon beta [sic alpha] protein." However, inspection of the amendment filed March 4, 2004, indicates that the word "has" was not deleted but appeared between two longer passages that were stricken. The above copy of claims reflects the current language for claim 1. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103(a)

Claims 1-3, 5-10, 13-14 and 17-21 are rejected under 35 U.S.C. 103 (a) as being unpatentable over DELTA BIOTECHNOLOGY LTD. (WO 97/24445 or KR99076789) ("Delta") in view of CETUS CORPORATION (EP 215,658) ("Cetus").

The Office alleges that Delta discloses serum albumin fusion proteins comprising the sequence set forth in SEQ ID NO: 18 of the instant application, that the albumin is useful as a component of a fusion protein because it is a stabilizer and transporter of

other proteins, and that the fusion proteins have an increased circulatory half-life (shelf life) over unfused proteins. However, the Office acknowledges that Delta does not disclose an interferon alpha protein according to the invention as now claimed. The Office further alleges that Cetus teaches the use of albumin to stabilize interferon alpha.

The Office's position is that one having ordinary skill in the art would be motivated to combine the teachings of the references to fuse interferon alpha with albumin to make an albumin fusion protein because Cetus teaches a composition wherein interferon alpha is stabilized by albumin and that native alpha-interferons are non-lipophilic proteins, which can be stabilized by adding a stabilizer such as albumin. Additionally, the Office points to Delta's alleged teaching on page 1 that albumin can be fused to therapeutic protein X wherein the therapeutic protein can be a polypeptide, antibody, peptide, fragments or variants thereof and that prolonged shelf-life is a benefit to having the protein in a fused state.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. MPEP § 706.02(j). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680 (Fed. Cir. 1990); MPEP § 2143.01. Moreover, the combination of references must provide some reasonable expectation of success for the claimed invention. MPEP § 2143.02. Here, neither reference cited by the Office teaches or suggests an albumin fusion protein of serum albumin or fragment thereof and an interferon alpha protein.

There is no objective reason to combine the teachings of the references, nor is there a reasonable expectation of success in obtaining the claimed invention as discussed below. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

The Office's stated motivations for combining Delta and Cetus are flawed and do not provide an objective reason for combining the reference teachings. First, as the Office admits, Delta does not teach or suggest a fusion protein comprising an interferon alpha protein. In fact, contrary to the Office's suggestions that Delta discloses albumin fusion proteins using any polypeptide, antibody, peptide, or fragments or variant thereof, Delta actually focuses on the fusion of albumin to human growth hormone. *See, e.g.,* Summary of Invention, pages 3-4. The only mention of therapeutic proteins other than growth hormone appears in the discussion of background prior art (pp. 1-3), which specifically notes problems identified in the prior art concerning fusion proteins of human serum albumin. *See* page 2, lines 1-3 and page 3, lines 21-23. This brief mention in the background section, which actually highlights the difficulties faced by the prior art in obtaining functional fusion proteins, does not motivate one of ordinary skill in the art to substitute a different protein such as an interferon alpha protein for the human growth hormone of Delta. Rather, this passage of Delta indicates that there would not be a reasonable expectation of success in obtaining the claimed invention.

The Office's main motivation for combining the two cited references appears to relate to broad statements in Cetus about stabilizing interferon alpha with albumin, which can only be found on page 4 of Cetus. Cetus actually focuses on stabilizing and solubilizing interferon beta. For example, Cetus describes the use of serum albumin as

a separate element added to "stabilize" and solubilize interferon beta in an aqueous formulation. *See, e.g.,* page 5, lines 10-20; page 6, lines 1-8; and page 9, line 13 to page 10, line 25. Cetus does not describe or even remotely suggest *a fusion protein* comprising these two separate elements nor does the Cetus reference suggest a fusion protein comprising serum albumin and interferon alpha. A person of ordinary skill in the art would not have been motivated to modify the teachings of Cetus in such a fundamental way in order to arrive at the claimed invention. Nor would a person of ordinary skill in the art be motivated to modify the teachings of Delta based on the teachings in Cetus relating to aqueous solutions.

There is no scientific basis in these references for suggesting that the albumin fusion proteins of Delta comprising human growth hormone are analogous to the Cetus aqueous solutions comprising, as separate elements, serum albumin and interferon alpha. Accordingly, there is no basis to conclude from these references that an interferon alpha protein would be useful in the context of albumin fusion proteins. It appears in this rejection that the Office is improperly employing hindsight construction based on Applicants' disclosure. *See In re Gordon*, 221 U.S.P.Q.2d 1125, 1127 (Fed. Cir. 1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.") Since the prior art relied upon in this rejection fails to establish a *prima facie* case of obviousness, this rejection should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: Charles E Van Horn
Charles E. Van Horn
Reg. No. 40,266

Dated: September 21, 2004